IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :

Greene et al.

Group No. : 1812

Appl. Serial No.: 08/469,637

Examiner : Pak, M.

Filed: June 6, 1995

Attorney Docket No. : 1488.0710001 (PF172P1)

For: **Human Tumor Necrosis Factor Receptor**

Declaration of John M. Greene and Robert D. Fleischmann Under 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

1. We, John M. Greene and Robert D. Fleischmann hereby declare and state as follows:

2. We are named inventors of the captioned application, which is assigned to Human Genome Sciences, Inc. (HGS). The work described below was done by ourselves, under our supervision, or as part of a collaborative research effort with other individuals at HGS.

3. As described in each of International application No. PCT/US95/03216, U.S. application Serial No. 08/469,637, and U.S. application Serial No. 08/718,737, we obtained a cDNA clone encoding human Tumor Necrosis Factor Receptor (TNF receptor) by screening a cDNA library derived from early passage human fibroblast HSA 172 cells (*See e.g.,* International application No. PCT/US95/03216, page 6). This clone was designated HSABH13. We have determined nucleotide sequence information for the HSABH13 clone, as described below, using sequencing methods which were routine and publicly available as of the March 15, 1995 filing date of the PCT/US95/03216 application. The HSABH13 clone that we obtained this sequence information from was deposited with the American Type Culture Collection (ATCC) on September 29, 1994 and was assigned ATCC Accession No. 75899 (*See* Attachment A).

4. Evidence that the human HSABH13 cDNA was deposited at the ATCC as Accession No. 75899 is provided in the second column of the IRIS notebook page included herewith as the first page of Attachment B[1]. In one instance, an "X" appears at the end of the HSABH13 clone identifier (see the first column on the notebook page). This HSABH13X designation represents the sequence identifier (SEQ ID) assigned to the sequence information of the first sequencing run. In a second instance, a "P" appears at the end of the same clone identifier. This HSABH13P designation represents the sequence identifier assigned to the sequence information of the second sequencing run. The second column of the notebook page provides two identifying numbers that are assigned by HGS scientists. From looking at the first and second columns together, it is clear that the HGS numbers provided, 195,197 and 1,261,140, represent different sequencing runs performed on the same human cDNA clone, HSABH13. HGS No. 195,197 appears as the identifier on the ATCC deposit receipt (*See* Attachment A). This indicates that the clone used to obtain the sequence information of HGS No.195,197 was deposited. In other words, even though, as explained below, the data derived from each sequencing run are not identical, the human HSABH13 cDNA clone used to obtain the data from each sequencing run was deposited at the ATCC and assigned Accession No. 75899.

5. The second, third and fourth pages of Attachment B provide data from the IRIS electronic notebook which shows the results from the HSABH13P sequencing run (hereinafter the "second sequencing run") on the human TNF receptor HSABH13 cDNA clone, which has been assigned Accession Number 75899. The nucleotide sequence information obtained from the second sequencing run of cDNA clone HSABH13 differs from that disclosed in Figures 1A and 1B of International application No. PCT/US95/03716 and U.S. application Serial No. 08/469,637, as filed (hereinafter referred to as the "first sequencing run"). The sequence disclosed in the second sequencing run, and the sequence disclosed in the first sequencing run were both obtained from the same HSABH13 clone (Accession No: 75899) using a 373 Automated DNA sequencer (Applied Biosystems, Inc.). Sequencing accuracy using this method is predicted to be greater than 97%.

6. The information obtained from the second sequencing run differs from that of the first sequencing run by including additional flanking regions (nucleotides 1-45 and 1217-1248) and deleting one nucleotide ("C") at position 1076 of the sequence derived from the first sequencing run, resulting in a frameshift for the remainder of the sequence. The amino acid sequence of human TNF receptor deduced from the information obtained in the second sequencing run differs from that deduced from the information obtained in the first sequencing run in that the amino

[1] IRIS is an electronic notebook used by HGS scientists to enter and maintain sequence data.

acids at positions 338-380 of the amino acid sequence deduced from the information obtained in the second sequencing run differ from the amino acids at positions 338-369 of the amino acid sequence deduced from the information obtained in the second sequencing run. This change in amino acids results from the frameshift in the nucleotide sequence described above.

7. The first sequencing run and second sequencing run data share more than 99% identity at the nucleotide level in the TNF receptor coding region, and more than 89% identity at the amino acid level.

8. International application No. PCT/US95/03216 and U.S. application Serial No. 08/469,637 were filed with the sequence data derived from the first sequencing run and U.S. application Serial No. 08/718,737 was filed with the sequence data derived from the second sequencing run.

9. We believe that the actual nucleotide sequence of the human cDNA clone HSABH13 (Accession No. 75899) is the same as that entered in the IRIS notebook for the second sequencing run.

10. We are of the opinion that the correct human TNF receptor nucleotide and amino acid sequences would have been apparent to one skilled in the art in possession of ATCC Deposit No. 75899 and the data from the second sequencing run as of the March 15, 1995 filing date of the PCT/US95/03216 application. This is so because the correct TNF receptor coding sequence can be readily determined from the deposited clone and methods for sequencing this clone were routine in the art in March of 1995.

11. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by find or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereupon.

Date	John M. Greene
3/12/98	Robert D. Fleischmann
Date	Robert D. Fleischmann